Verastem Oncology Announces Preclinical Presentations for New Oral G12D Inhibitor and for Avutometinib and Defactinib Combination as a Backbone of Therapy for RAS/MAPK Driven Cancers at AACR Annual Meeting 2024

March 5, 2024 at 4:30 PM EST

GFH375 (VS-7375), a potential best-in-class oral KRAS G12D (ON/OFF) inhibitor, demonstrated potent anti-tumor activity in pancreatic and colorectal cancer models; Partner GenFleet plans to submit IND in H1 2024

Preclinical data demonstrate strong anti-tumor activity of avutometinib with FAK inhibitor combination with standard-of-care chemotherapy in pancreatic cancer models; supports the scientific rationale for ongoing RAMP 205 Phase 1/2 trial

Avutometinib with FAK inhibitor combination overcomes resistance to BRAF and MEK inhibitors and to immunotherapy in patient-derived melanoma models

BOSTON--(BUSINESS WIRE)--Mar. 5, 2024-- Verastem Oncology (Nasdaq: VSTM), a biopharmaceutical company committed to advancing new medicines for patients, today announced that preclinical data will be presented in five posters at the American Association for Cancer Research (AACR) Annual Meeting 2024 to be held on April 5-10 in San Diego, California. The presentations will highlight anti-tumor efficacy of GFH375 (VS-7375), a potent and selective orally bioavailable KRAS G12D (ON/OFF) inhibitor, and will also show data of RAF/MEK clamp plus FAK inhibition in pancreatic ductal adenocarcinoma (PDAC) models supporting the ongoing RAMP 205 trial. Additional presentations will support the use of avutometinib and FAK inhibitor combination in cutaneous melanoma models to overcome resistance to BRAF and MEK inhibitors, resistance to immunotherapy, and brain metastasis.

“For the first time, GenFleet and Verastem will present potency, selectivity, anti-tumor efficacy, and bioavailability data on GFH375 (VS-7375), a potential best-in-class orally active KRAS G12D (ON/OFF) inhibitor. We look forward to an IND submission by GenFleet in China in H1 2024,” said Jonathan Pachter, Ph.D., chief scientific officer of Verastem Oncology. “Additionally, preclinical data will be presented demonstrating that the combination of avutometinib and a FAK inhibitor with standard-of-care chemotherapy can induce tumor regressions in pancreatic cancer models, providing the scientific rationale for the ongoing RAMP 205 Phase 1/2 study evaluating the combination of avutometinib, defactinib, gemcitabine, and nab-paclitaxel in first-line metastatic pancreatic ductal adenocarcinoma. Collectively, these data from the five posters build on our desire to advance treatments that target the RAS/MAPK pathway and provide new options for patients with RAS/MAPK driven cancers.”

Key Data Presentations:

- **Title:** GFH375 (VS-7375): An oral, selective KRAS G12D (ON/OFF) inhibitor with potent anti-tumor efficacy
- **Abstract #:** 3318
- **Date/Time:** Monday, April 8, 2024, 1:30 – 5:00 p.m. PDT
- **Sponsor:** GenFleet Therapeutics

- **Title:** Combined inhibition of RAF, MEK and FAK increases PDAC responsiveness to cytotoxic- and immune therapy
- **Abstract #:** 2899
- **Date/Time:** Monday, April 8, 2024, 1:30 – 5:00 p.m. PDT
- **Institution**: Siteman Cancer Center, Department of Medicine, Washington University School of Medicine

- **Title:** Combined Inhibition of RAF, MEK, and FAK attenuates melanoma brain metastases and prolongs survival in preclinical models
- **Abstract #:** 4127
- **Date/Time:** Tuesday, April 9, 2024, 9:00 a.m. – 12:30 p.m. PDT
- **Institution**: Huntsman Cancer Institute, Department of Surgery, University of Utah School of Medicine

- **Title:** A novel combination therapy targeting RAF, MEK, and FAK to overcome skin cutaneous melanoma treatment resistance
- **Abstract #:** 4745
- **Date/Time:** Tuesday, April 9, 2024, 9:00 a.m. – 12:30 p.m. PDT
- **Institution**: Moores Cancer Center-Department of Pharmacology, University of California San Diego

- **Title:** The SOS1 Inhibitor MRTX0902 Demonstrates Activity Across Cancer Models with Mutations in Proximal

Components of the RAS-MAPK pathway
- **Abstract #:** 7268
- **Date/Time:** Wednesday, April 10, 2024, 9:00 a.m. – 12:30 p.m. PDT
- **Sponsor**: Mirati Therapeutics, Inc.

The accepted abstracts are available on the AACR conference website: https://www.aacr.org/meeting/aacr-annual-meeting-2024/.

About GFH375 (VS-7375)

GFH375 (VS-7375) is a potential best-in-class, potent and selective oral KRAS G12D (ON/OFF) inhibitor, identified as the lead program from the Verastem Oncology discovery and development collaboration with GenFleet Therapeutics. GenFleet plans to submit an IND in China for GFH375 (VS-7375) in the first half of 2024, and upon approval GenFleet is expected to initiate a Phase 1 trial in China in the second half of 2024. The collaboration includes three discovery programs, the first being the KRAS G12D inhibitor, and will provide Verastem Oncology with exclusive options to obtain licenses to each of the three compounds in the collaboration after successful completion of pre-determined milestones in Phase 1 trials. The licenses would give Verastem Oncology development and commercialization rights outside of the GenFleet markets of mainland China, Hong Kong, Macau, and Taiwan.

About the Avutometinib and Defactinib Combination

Avutometinib is a RAF/MEK clamp that induces inactive complexes of MEK with ARAF, BRAF and CRAF potentially creating a more complete and durable anti-tumor response through maximal RAS/MAPK pathway inhibition. In contrast to currently available MEK-only inhibitors, avutometinib blocks both MEK kinase activity and the ability of RAF to phosphorylate MEK. This unique mechanism allows avutometinib to block MEK signaling without the compensatory activation of MEK that appears to limit the efficacy of other MEK-only inhibitors. The U.S. Food and Drug Administration (FDA) granted Breakthrough Therapy designation for the combination of Verastem Oncology's investigational RAF/MEK clamp avutometinib, with defactinib, a selective FAK inhibitor, for the treatment of all patients with recurrent low-grade serous ovarian cancer (LGSOC) regardless of KRAS status after one or more prior lines of therapy, including platinum-based chemotherapy.

Verastem Oncology is currently conducting clinical trials with its RAF/MEK clamp avutometinib in RAS/MAPK driven tumors as part of its (**R**af **A**nd **M**ek **P**rogram). RAMP 301 (NCT06072781) is a Phase 3 confirmatory trial evaluating the combination of avutometinib and defactinib versus standard chemotherapy or hormonal therapy for the treatment of recurrent LGSOC. RAMP 201 (NCT04625270) is a Phase 2 registration-directed trial of avutometinib in combination with defactinib in patients with recurrent LGSOC and has completed enrollment in the dose optimization, expansion phase, and low-dose evaluation cohorts.

Verastem Oncology has established clinical collaborations with Amgen and Mirati to evaluate LUMAKRAS™ (sotorasib) and KRAZATI™ (adagrasib) in combination with avutometinib in KRAS G12C mutant NSCLC as part of the RAMP 203 (NCT05074810) and RAMP 204 (NCT05375994) trials, respectively. Supported by the "Therapeutic Accelerator Award" Verastem Oncology received from PanCAN, the Company is conducting RAMP 205 (NCT05669482), a Phase 1b/2 clinical trial evaluating avutometinib and defactinib with gemcitabine/nab-paclitaxel in patients with front-line metastatic pancreatic cancer.

About Verastem Oncology

Verastem Oncology (Nasdaq: VSTM) is a late-stage development biopharmaceutical company committed to the development and commercialization of new medicines to improve the lives of patients diagnosed with cancer. Our pipeline is focused on novel small molecule drugs that inhibit critical signaling pathways in cancer that promote cancer cell survival and tumor growth, including RAF/MEK inhibition and FAK inhibition. For more information, please visit www.verastem.com and follow us on LinkedIn.

Forward-Looking Statements Notice

This press release includes forward-looking statements about Verastem Oncology's strategy, future plans and prospects, including statements related to the expected outcome and benefits of the collaboration with GenFleet, Amgen and Mirati, the potential clinical value of various of its clinical trials, the timing of commencing and completing trials, including topline data reports, interactions with regulators and the potential for and timing of commercialization of product candidates. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," "can," "promising" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement.

Applicable risks and uncertainties include the risks and uncertainties, among other things, regarding: the success in the development and potential commercialization of our product candidates, including avutometinib in combination with other compounds, including defactinib, LUMAKRAS™ and others; the uncertainties inherent in research and development, such as negative or unexpected results of clinical trials, the occurrence or timing of applications for our product candidates that may be filed with regulatory authorities in any jurisdictions; whether and when regulatory authorities in any jurisdictions may approve any such applications that may be filed for our product candidates, and, if approved, whether our product candidates will be commercially successful in such jurisdictions; our ability to obtain, maintain and enforce patent and other intellectual property protection for our product candidates; the scope, timing, and outcome of any legal proceedings; decisions by regulatory authorities regarding trial design, labeling and other matters that could affect the timing, availability or commercial potential of our product candidates; whether preclinical testing of our product candidates and preliminary or interim data from clinical trials will be predictive of the results or success of ongoing or later clinical trials; that the timing, scope and rate of reimbursement for our product candidates is uncertain; that third-party payors (including government agencies) may not reimburse; that there may be competitive developments affecting our product candidates; that data may not be available when expected; that enrollment of clinical trials may take longer than expected; that our product candidates will cause adverse safety events and/or unexpected concerns may arise from additional data or analysis, or result in unmanageable safety profiles as compared to their levels of efficacy; that our product candidates may experience manufacturing or supply interruptions or failures; that any of our third party contract research organizations, contract manufacturing organizations, clinical sites, or contractors, among others, who we rely on fail to fully perform; that we face substantial competition, which may result in others developing or commercializing products before or more successfully than we do which could result in reduced market share or market potential for our product candidates; that we will be unable to successfully initiate or complete the clinical development and eventual commercialization of our product candidates; that the development and commercialization of our product candidates will take longer or cost more than planned, including as a result of

conducting additional studies; that we may not have sufficient cash to fund our contemplated operations; that we may not attract and retain high quality personnel; that we or Chugai Pharmaceutical Co., Ltd. will fail to fully perform under the avutometinib license agreement; that our target market for our product candidates might be smaller than we are presently estimating; that Secura Bio, Inc. will fail to fully perform under the asset purchase agreement with Secura Bio, Inc., including in relation to milestone payments; that we will not see a return on investment on the payments we have and may continue to make pursuant to the collaboration and option agreement with GenFleet or that GenFleet will fail to fully perform under the agreement; that we may be unable to obtain adequate financing in the future through product licensing, co-promotional arrangements, public or private equity, debt financing or otherwise; that we will not pursue or submit regulatory filings for our product candidates; and that our product candidates will not receive regulatory approval, become commercially successful products, or result in new treatment options being offered to patients.

Other risks and uncertainties include those identified under the heading “Risk Factors” in the Company’s Annual Report on Form 10-K for the year ended December 31, 2022 as filed with the Securities and Exchange Commission (SEC) on March 14, 2023 and in any subsequent filings with the SEC. The forward-looking statements contained in this press release reflect Verastem Oncology’s views as of the date hereof, and the Company does not assume and specifically disclaims any obligation to update any forward-looking statements whether as a result of new information, future events or otherwise, except as required by law.

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